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10/533,555	05/02/2005	Wei Xu	EX03-037C-US	9452	
	63572 7590 07/29/2008 MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP			EXAMINER	
300 SOUTH WACKER DRIVE			MABRY, JOHN		
SUITE 3100 CHICAGO, IL 60606			ART UNIT	PAPER NUMBER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)			
	10/533,555	XU ET AL.			
Office Action Summary	Examiner	Art Unit			
	John Mabry, PhD	1625			
The MAILING DATE of this communication app Period for Reply	pears on the cover sheet with the c	orrespondence address			
A SHORTENED STATUTORY PERIOD FOR REPL WHICHEVER IS LONGER, FROM THE MAILING D  - Extensions of time may be available under the provisions of 37 CFR 1.1 after SIX (6) MONTHS from the mailing date of this communication.  - If NO period for reply is specified above, the maximum statutory period - Failure to reply within the set or extended period for reply will, by statute Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION (36(a). In no event, however, may a reply be tin will apply and will expire SIX (6) MONTHS from e, cause the application to become ABANDONE	N. nely filed the mailing date of this communication. D (35 U.S.C. § 133).			
Status					
<ul> <li>1) Responsive to communication(s) filed on 05 M</li> <li>2a) This action is FINAL. 2b) This</li> <li>3) Since this application is in condition for alloware closed in accordance with the practice under E</li> </ul>	s action is non-final. nce except for formal matters, pro				
Disposition of Claims					
4) Claim(s) 1-9,12-19,24 and 27-38 is/are pendin 4a) Of the above claim(s) 24-30 is/are withdray 5) Claim(s) is/are allowed. 6) Claim(s) 1-9,12-19 and 31-38 is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and/o Application Papers  9) The specification is objected to by the Examine 10) The drawing(s) filed on is/are: a) accomposite and applicant may not request that any objection to the Replacement drawing sheet(s) including the correct 11) The oath or declaration is objected to by the Examine 11.	wn from consideration.  or election requirement.  er. eepted or b) □ objected to by the I drawing(s) be held in abeyance. See tion is required if the drawing(s) is objected.	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).			
Priority under 35 U.S.C. § 119					
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  a) All b) Some color None of:  1. Certified copies of the priority documents have been received.  2. Certified copies of the priority documents have been received in Application No  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  * See the attached detailed Office action for a list of the certified copies not received.					
Attachment(s)  1) Notice of References Cited (PTO-892)  2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 5/2/05, 6/20/05.	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	ate			

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#### **DETAILED ACTION**

## Examiner's Response

Applicant's response on May 5, 2008 filed in response to the Election/Restriction dated February 4, 2008 has been received and duly noted. The Examiner acknowledges Applicants' election of Group II with traverse. The Applicant requested that Groups I-VIII be examined together. The Applicant alleges that the Examiner improperly restricted the instant application. Applicant points out the Tang reference (US 6,689,806) that the Examiner used to break the unity of invention does not fall within the scope of Applicant's Formula I. Examiner does not agree to this allegation. According to Applicant's Formula I of instant application and definitions therein, Tang discloses compound of Formula I wherein W=CR1 where R1=H, K=O, R2=H, X=phenyl and substituted pyrrole where L=NH, Q=CH and R5=CH3.

Tang et al (US 6,316,429 B1) discloses structural similar compounds of Formula I and teaches (L=S) and (L and Q=N) (see below and column 6).

It would be obvious to combine the references of US '806 and '429 to achieve the instant claimed invention.

Examiner has rejoined and examined Groups I-III. Examiner's Election/Restriction was properly restricted and Groups IV-VIII were not considered in this Office Action.

Thus, the restriction requirement is deemed proper and <u>FINAL</u>.

In view of this response, the status of the rejections/objections of record is as follows:

Applicant is respectfully reminded that it is <u>required</u> that all claims be amended to elected group. Examiner also warns Applicant not to introduce new matter when amending.

#### Specification Objections

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The current title is "Kinase Modulators". Examiner suggests a title that directed towards elected group.

### Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 12-19 and 31-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R13 being H, alkoxy, amino, alkylamino and heteroalicyclic where heteroalicyclic compounds are morpholino, pyrrolidinyl and piperidinyl; R4 and R5 fused to form phenyl; and R10 being H, alkyl,

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alkoxy, cyano, halo, haloakyl does <u>not</u> reasonably provide enablement for R13 being all claimed heteroalicyclic compounds, R4 and R5 being all fused cyclic rings claimed and R10 being all substituents as claimed.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The Specification does not provide any support for said variables at R13, R10 and R4/R5 positions. Pages 65-78 of the Specification describe starting materials and methods for synthesis of compounds as described above, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where R13, R10 and R4/R5 positions as listed above.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

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The analysis is as follows:

(1) Breadth of claims: Scope of the compounds. Owing to the range of many variables,

millions of highly substituted indolin-2-one compounds are embraced.

(2) The nature of the invention: The invention is a highly substituted indolin-2-one

compounds.

(3) Level of predictability in the art: It is well established that "the scope of enablement

varies inversely with the degree of unpredictability of the factors involved," and chemical

reactivity (which is affected by determinants such as substituent effects, steric effects,

bonding, molecular geometry, etc) is generally considered to be an unpredictable factor.

See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(4) Direction or Guidance: That provided is very limited. Applicant shows a general

synthesis of compounds of application's general formula I. Pages 65-78 of the

Specification describes starting materials and methods for synthesis of compounds

wherein R13, R10 and R4/R5 positions, but does not describe or list any reagents

wherein compounds can be used to synthesis compounds where R13, R10 and R4/R5

positions as listed above. There is limited evidence in the Specification of the example

compounds that only covers no or a small portion of the substituents claimed of formula

I. Thus, there is no specific direction or guidance regarding said compounds specifically

mentioned in Scope.

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The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court *in re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

(5) State of the Prior Art: These compounds are substituted indolin-2-one compounds wherein R13 being H, alkoxy, amino, alkylamino and heteroalicyclic where heteroalicyclic compounds are morpholino, pyrrolidinyl and piperidinyl; R4 and R5 fused to form phenyl; and R10 being H, alkyl, alkoxy, cyano, halo, haloakyl. So far as the examiner is aware, no substituted indolin-2-one compounds of general formula I wherein R1 equals all claimed heteroalicyclic compounds, R4 and R5 being all fused cyclic rings claimed and R10 being all substituents as claimed have been made or used.

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It is not trivial to experimentally interchange any and all of the many substituents that exist. As described by F. Zaragoza Dörwald, most organic syntheses fail initially and chemical research is highly inefficient due to chemists spending most of their time "finding out what went wrong and why". Therefore, most syntheses of organic compounds are labor-intensive and demanding. Additionally, most final synthetic routes to desired organic molecules are usually very different from initially planned routes. A highly skilled chemist can agree that for many successful organic compounds made, many failures are encountered and experimental repetition is common. This also contributes to the burden and unpredictability of the syntheses of said compounds. (see "Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design" 2005 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

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- (6) Working Examples: Applicant shows examples (Table 2 on pages 54-63) but no working examples were shown wherein R13, R10 and R4/R5 positions equal aforementioned substituents and chemical moieties have been made or used of any kind.
- (7) Skill of those in the art: The ordinary artisan is highly skilled, e.g. a masters or PhD level chemist.
- (8) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high

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and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

#### Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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Claims 1-9, 12-19 and 31-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang (US 6,689,806) in view of Tang (US 6,316,429 B1) (PTO-1449) and in further view of US 6,569,868 (PTO-1449).

The instant application discloses compounds and pharmaceutical compositions of Formula I as disclosed below wherein R10=OCH3, R5=H, R6=CH3 and R12=CH3 and R13=H.

# Scope & Content of Prior Art MPEP 2141.01

Tang (US 6,689,806) compounds and pharmaceutical compositions of Formula I as disclosed below wherein R10=OCH3, R5=H and R6=CH3.

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Tang et al (US 6,316,429 B1) discloses structural similar compounds of Formula I and teaches (Q=CH) and (L=N) (see below and column 6).

Tang (US '429) teaches the indole ring can be substituted with:

This teaching is found in column 5, lines 38-49 where R4 of US '429 can be –NR10R11 wherein R10 = H and R11 = piperidinyl substituted with alkyl.

#### Differences between Prior Art & the Claims MPEP 2141.02

US '806 differs from instant application at: (a) the 5-membered N containing

heteroaryl compound:

which are positional isomers

and (b) the phenyl substitution on the indole ring in which there is a clear teaching as described above.

(a) There is little difference between the imidazole being bonded to the 4-position as compared at the 2-position on the claimed structure of formula I. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be prepared by the same

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method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt*, 208 USPQ 343, 349; *In re Mehta*, 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ullyot*, 103 USPQ 185; *In re Norris*, 84 USPQ 459; *Ex. Parte Naito*, 168 USPQ 437, 439; *Ex parte Allais*, 152 USPQ 66; *In re Wilder*, 166 USPQ 545, 548; *Ex parte Henkel*, 130 USPQ 474; *Ex parte Biel*, 124 USPQ 109; *In re Petrzilka*, 165 USPQ 327; *In re Crownse*, 150 USPQ 554; *In re Fouche*, 169 USPQ 431; *Ex parte Ruddy*, 121 USPQ 427; *In re Wiechert*, 152 USPQ 249, *In re Shetty*, 195 USPQ 753; *In re Jones*, 74 USPQ 152, 154. There may be others as well. Thus, said claims are rendered obvious by Tang et al.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (*Englehardt*) and "Position isomerism is fact of close structural similarity" (*Mehta*, emphasis in the original). Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to prima facie obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers." Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new

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compounds...a known compound may suggest it analog or isomers, either geometric (cis v. trans) or position isomers (e.g. *ortho v. para*)." See also MPEP 2144.09, second paragraph. Further, the reference provides for the ring being substituted in any position.

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# Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

It would be obvious to combine the references of US '806 and '429 to achieve the instant claimed invention. An artisan of ordinary skill would be motivated to use (and obvious to try) US '806 which teaches the core of the claimed genus of Formula I and combine it with the teachings of US '429 in order to treat/modulate/inhibit the activity of a protein kinase as taught by both mentioned US patent references.

Additionally, US '806 teaches the phenyl ring substitution where R13-R16 can be NR25R26, wherein R25 is H and R26 is heteroaryl (see column 13).

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$$\begin{array}{c} R_{23} \\ R_{23} \\ R_{16} \\ R_{18} \\ \end{array}$$

25

or a physiologically acceptable salt or prodrug thereof where P is 0 or 1.

When p is 1, then M, Q, T, U and V are independently selected from the group consisting of carbon and nitrogen, it being understood that, when M, Q, T, U, or V is nitrogen, 30 R<sub>200</sub>, R<sub>210</sub>, R<sub>220</sub>, R<sub>220</sub>, or R<sub>240</sub>, respectively, do not exist.

R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, or R<sub>24</sub>, respectively, do not exist.

When p is 0, then M, Q, U, and V are independently selected from the group consisting of carbon, nitrogen, oxygen and sulfur, it being understood that, when M, Q, U, or V is oxygen or sulfur or nitrogen (wherein said nitrogen 35 is participating in a double bond), R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, or R<sub>24</sub>, respectively, do not exist.

R<sub>16</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, or R<sub>24</sub> are independently selected from the group consisting of hydrogen, aikyl, trihaioaikyl, cycloalkyl, aikenyl, aikynyl, 40 aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, mercapto, alkylthio, aryloxy, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, carbonyl, C-carboxy, O-carboxy, carboxyaikyl, cyano, nitro, halo, O-carbamyl, N-carbamyl, C-amido, N-amido and —NR<sub>25</sub>R<sub>26</sub>.

 $R_{20}$  and  $R_{21}$  or  $R_{21}$  and  $R_{22}$  or  $R_{23}$  and  $R_{24}$  or  $R_{23}$  and  $R_{24}$  may combine to form a five-member or a six-member aryl or heteroaryl ring.

 $R_{25}$  and  $R_{26}$  are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, 50 aryl, heteroaryl, carbonyl, sulfonyl, and, combined, a five-member or a six-member heteroalicyclic ring.

US 6,569,868 (PTO-1449) discloses species and teachings as claimed in the instant application (claims 1-9, 12-19 and 31-38). US '868 provides further support that compounds and teachings of similar structures of the instant invention are well known in the prior art.

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The scope of this invention includes physiologically acceptable saits and produigs of the compounds claimed herein.

A, B, D and E are independently selected from the group consisting of carbon and nitrogen wherein it is understood that, when A, B, D or E is nitrogen, R<sup>2</sup>, R<sup>3</sup>, R<sup>8</sup> or R<sup>2</sup>, respectively, does not exist and there is no bond.

G and J are selected from the group consisting of nitrogen and carbon such that, when G is nitrogen, J is carbon and when J is nitrogen, G is carbon. When either G or J is nitrogen then  $\mathbb{R}^5$  or  $\mathbb{R}^5$ , respectively, does not exist.

R<sup>2</sup> and the imidazolyl ring may exchange places on the double bond; i.e., compound 1 may exist in the E or Z configuration about the double bond at the 3-position of the 2-indolinous.

R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, C-amido, C-thioamido, suifonyl and tribalomethylsulfonyl.

 $\hat{R}^2$  is selected from the group consisting of hydrogen, alkyl, cycloaikyl, aryl, beteroaryl and halo.

R\*, R\*and R\*: are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, halo, irihalomethyl, hydroxy, alkoxy, aryloxy, C-carboxy, O-carboxy, carbonyl, nitro, avano, S-sulforamido, amino and —NR 20R 12.

nitro, cyano, S-sulforamido, amino and —NR<sup>15</sup>R<sup>11</sup>.

R<sup>10</sup> and R<sup>13</sup> are independently selected from the group consisting of alkyl, cycloalkyl, aryl, carbonyl, sulfonyl, trihalomethanesulfonyl and, combined, a five-member or a six-member heteroalicyclic ring.

R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are independently selected from the group consisting of hydrogen, alkyl, trihaloslkyl, cyclosikyl, slkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, slkoxy, aryloxy, thiohydroxy, thioslkoxy, thiosryloxy, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, N-trihalomethanesulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, cyanato, isocyanato, thiocyanato, isothiocyanato, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino and —NR<sup>10</sup>R<sup>12</sup>.

R<sup>6</sup> and R<sup>7</sup> or R<sup>7</sup> and R<sup>6</sup> or R<sup>8</sup> and R<sup>9</sup>, combined, may form a five or six-membered atomatic, beteroaromatic, alicyclic or heteroalicyclic ring such as, by way of example and not limitation, a methylenedioxy or an ethylenedioxy ring.

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The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR, 550 U.S. at\_\_\_\_, 82 USPQ2d at 1396. Exemplary rationales that may support a conclusion of obviousness include:

- (A) Combining prior art elements according to known methods to yield predictable results;
- (B) Simple substitution of one known element for another to obtain predictable results;
- (C) Use of known technique to improve similar devices (methods, or products)in the same way;
- (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
- (E) "Obvious to try" choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
- (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

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(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. See MPEP § 2143 for a discussion of the rationales listed above along with examples illustrating how the cited rationales may be used to support a finding of obviousness. See also MPEP § 2144- §2144.09 for additional guidance regarding support for obviousness determinations.

The aforementioned reasons above describe rationales that support a conclusion of obviousness based upon the KSR International Co. v. Teleflex Inc. decision. Letters (A)-(G) rationale is supported above.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Conclusion

Applicant is respectfully reminded that it is required that all claims be amended to

elected group. Examiner also warns Applicant not to introduce new matter when

amending.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to John Mabry, PhD whose telephone number is (571)

270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's

primary examiner can be reached at (571) 272-0684, first, or the Examiner's supervisor,

Janet Andres, PhD, can be reached at (571) 272-0867. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/ Examiner

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/Rita J. Desai/ Primary Examiner, Art Unit 1625